REMARKS/ARGUMENTS

The Status of Claims

Claims 1-25, 27-39, 42-63, and 65-77 were pending in the present application before the Amendment as set forth above. By the Amendment, claims 1, 5-7, 49, 53 and 76 are amended and claims 4, 8, 52, and 56 are canceled without prejudice.

In the July 12, 2010 Office Action (hereinafter "the Office Action"), claims 1-8, 13-18, 20-23, 25, 27-31, 39, 42-44, 48-56, 61, 63, 65-69, 71 and 75 were rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Publication No. 2003/0003571 to Kanegasaki (hereinafter "Kanegasaki"), in view of U.S. Patent No. 5,520,787 to Hanagan and U.S. Patent No. 5,589,352 to Breznak (hereinafter "Breznak"). In addition, claims 9-12 and 57-60 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of U.S. Patent No. 6,197,575 to Griffith et al. (hereinafter "Griffith") or U.S. Patent Application Publication No. 2006/0194273 to Thomas (hereinafter "Thomas"). Also, claims 19 and 24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of U.S. Patent No. 2,157,438 to Sparks (hereinafter "Sparks"). Further, claims 32 and 70 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of U.S. Patent No. 6,391,558 to Henkens et al. (hereinafter "Henkens"). Still further, claims 33-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of U.S. Patent Application Publication No. 2002/0164816 to Quake (hereinafter "Quake"). In addition, claims 45, 46, 72, and 73 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegaski, in view of Hanagan and Breznak, and further in view of U.S. Patent Application Publication No. 2002/0025547 to Rao (hereinafter "Rao") or U.S. Patent Application Publication No. 2004/0142409 to Allen (hereinafter "Allen"). Also, claims 47 and 74 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegaski, in view of Hanagan and Breznak, and further in view of U.S. Patent No. 6,168,948 to Anderson et al. (hereinafter "Anderson"). Further, claim 76 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki,

in view of U.S. Patent Publication No. 2001/0044143 to Herman et al. (hereinafter "Herman"). Still further, claim 77 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegaski, in view of Herman, and further in view of U.S. Patent No. 5,624,537 to Turner et al. (hereinafter "Turner").

The Telephone Interview

Applicant very much appreciates the Examiner's careful review of the instant application. Applicant particularly thanks Examiner Edwards and Supervisory Examiner Griffin for granting and conducting a telephone interview on August 17, 2010. Applicant also appreciates very much the professionalism shown by Examiner Edwards and Supervisory Examiner Griffin during the telephone interview. In the telephone interview, the July 12, 1010 Office Action was discussed, and particularly independent claims 1, 49, and 76 of the present invention and the cited references to Kanegasaki, Hanagan, Breznak, and Herman. The Examiner and Supervisory Examiner suggested amendments to further the prosecution of the present application.

The Response

In response, as set forth above, claims 1, 5-7, 49, 53 and 76 have been amended for better form and according to the Examiner's suggestions. For example, features of originally filed claims 4 and 8, now canceled, have been incorporated into amended claim 1, and features of originally filed claims 52 and 56, now canceled, have been incorporated into amended claim 49. Without acquiescing to the propriety of the Examiner's rejections, as set forth above, claims 4, 8, 52, and 56 have been canceled without prejudice, which renders the Examiner's rejections under 35 U.S.C. § 103 moot. Applicant reserves every right in these canceled claims to file continuation applications.

Support for the amendments can be found in the disclosure as originally filed, for example in the claims as originally filed, in paragraphs on page 12, lines 28-38 through page 25, lines 1-3 of the specification and in Figs. 1-5 of the drawings, and more particularly in paragraphs on page 17, lines 20-28 and page 19, lines 28-38 through page 21, lines 1-15

of the specification and Figs. 1-5 of the drawings. Applicant submits that no new matter has been added.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical correction only.

It is now believed that the application is in condition for allowance at least for the reasons set forth below and such allowance is respectfully requested.

The following remarks herein are considered to be responsive thereto.

Rejections under 35 U.S.C. § 103

In the July 12, 2010 Office Action, claims 1-8, 13-18, 20-23, 25, 27-31, 39, 42-44, 48-56, 61, 63, 65-69, 71 and 75 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak. In addition, claims 9-12 and 57-60 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of Griffith or Thomas. Also, claims 19 and 24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of Sparks. Further, claims 32 and 70 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hangan and Breznak, and further in view of U.S. Henkens. Still further, claims 33-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Hanagan and Breznak, and further in view of Quake. In addition, claims 45, 46, 72, and 73 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegaski, in view of Hanagan and Breznak, and further in view of Rao or Allen. Also, claims 47 and 74 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegaski, in view of Hanagan and Breznak, and further in view of Anderson. Further, claim 76 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Herman. Still further, claim 77 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegaski, in view of Herman, and further in view of Turner.

Applicant respectfully traverses the rejections for at least the reasons set forth below.

Claims 1-3, 5-7, 9-25, 27-39, and 42-48:

As set forth above, amended claim 1 recites "[a] bioreactor comprising:

(a) a substrate having a first surface and an opposite second surface, defining a channel therein;

(b) a plurality of chambers formed in the substrate, wherein ***each of the plurality of chambers is adapted for receiving and culturing at least one predetermined type of cells*** in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end;

(c) means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers;

(d) ***a barrier for at least one of the chambers, wherein the barrier:***

(i) is positioned at the open end of the corresponding chamber and proximate to the intersection of the channel and the corresponding chamber; and

(ii) has a porosity to allow the corresponding chamber and the channel to be in fluid communication, and to allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined type of cells not to permeate between the corresponding chamber and the channel." (Emphasis added.)

In one embodiment of the present invention as shown in Figs. 1A and 1B of the drawings, a bioreactor 200 includes a barrier 209 for at least one of the chambers 206, where each of the plurality of chambers 206 "is adapted to receive and culture at least one ***predetermined type of cells,***" and where the predetermined type(s) of cells include, but are not limited to "***bacteria, protozoa, or both, normal cells, tumor cells, or any combination of them***." (Page 20, lines 17-

22.) (Emphasis added.) As shown in Fig. 1B, ***the barrier 209 is positioned at the open end 262 of a corresponding chamber 206 and proximate to an intersection of channel 202 and the corresponding chamber 206***. The barrier 209 has a porosity to allow the corresponding chamber 206 and the channel 202 to be in fluid communication with each other. Also, the barrier 209 ***allows at least one predetermined type of cells to permeate*** between the corresponding chamber 206 and the channel 202 and ***at least another predetermined type of cells not to permeate*** between the corresponding chamber 206 and the channel 202. Thus, the barrier 209 has a ***selective porosity*** for the cells and functions as a filter, as well, and may include a ***nanofilter*** (see page 17, lines 20-28 of specification as originally filed).

In contrast, as understood by Applicant, Kanegasaki discloses "a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor." (Kanegasaki, [00090].) In Kanegasaki, ***grooves or terraces***, for example, grooves 5 on a bank 10 in a channel 1 (see, e.g. Figs. 2, 4 and 6) are used for controlling position-adjustment of cells in the wells. (See also Kanegasaki, [0097].) The grooves have a width and/or a depth configured according to the ***diameter or deformability of cells provided***, where the "deformity of cells" refers to flexible cells that are able to easily change their shape and thus are able to pass through a gap with a smaller size than the diameter of the cells being in the inherent spherical shape in a free space. (Kanegasaki, [0084].)

Kanegasaki does not disclose, teach, or suggest bioreactor comprising: "a substrate having a first surface and an opposite second surface, defining a channel therein; a plurality of chambers formed in the substrate, wherein ***each of the plurality of chambers is adapted for receiving and culturing at least one predetermined type of cells*** in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end; means adapted for electrochemical measurements of the

cells responsive to the liquid medium in at least one of the chambers; ***a barrier for at least one of the chambers, wherein the barrier: is positioned at the open end of the corresponding chamber and proximate to the intersection of the channel and the corresponding chamber; and has a porosity to allow the corresponding chamber and the channel to be in fluid communication, and to allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined type of cells not to permeate between the corresponding chamber and the channel***," as recited in amended claim 1 of the present invention. (Emphasis added.)

The Examiner attempts to cure the deficiencies of Kanegasaki with the disclosures of Hanagan and Breznak. Hanagan, as understood by Applicant, discloses "a diagnostic flow cell for determining the presence or amount of an analyte in a test sample…[comprising] (i) a spacing layer disposed between a first and a second opposed substrate, wherein the spacing layer has a longitudinal void and wherein the spacing layer and opposed substrates define a flow channel; (ii) fastening means for coupling the spacing layer and the opposed substrates; (iii) inlet means for permitting a sample to enter the flow channel; (iv) outlet means for permitting the sample to exit the flow channel; and (v) immobilized reagent means for producing a detectible signal, wherein the reagent means is at least partially contained within the flow channel." (Hanagan, Col. 1, lines 54-66.) Breznak, as understood by Applicant, discloses a system and method for "observation of microorganisms in a controlled environment" using a diffusion gradient chamber with reservoirs. (Breznak, Abstract.)

Neither Hanagan nor Breznak, taken alone or in combination with Kanegasaki, disclose, teach, or suggest bioreactor comprising: "a substrate having a first surface and an opposite second surface, defining a channel therein; a plurality of chambers formed in the substrate, wherein ***each of the plurality of chambers is adapted for receiving and culturing at least one predetermined type of cells*** in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end;

means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers; ***a barrier for at least one of the chambers, wherein the barrier: is positioned at the open end of the corresponding chamber and proximate to the intersection of the channel and the corresponding chamber; and has a porosity to allow the corresponding chamber and the channel to be in fluid communication, and to allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined type of cells not to permeate between the corresponding chamber and the channel***," as recited in amended claim 1 of the present invention. (Emphasis added.)

For at least the reasons set forth above, Applicant respectfully submits that the Examiner has failed to make a *prima facie* case to support the rejection of claim 1 under 35 U.S.C. §103(a) over Kanegasaki, Hanagan, and/or Breznak, taken alone or in combination. First, there is no suggestion or motivation to modify the references or combine the reference teachings. Second, there is no reasonable expectation of success of combining the reference teachings. Finally, the combination of references does not teach or suggest all elements of Applicant's claims.

In supporting the obviousness rejections under 35 U.S.C. §103, the Examiner "bears ***the initial burden…of presenting a prima facie case of unpatentability***…After evidence or argument is submitted by the applicant in response, patentability is determined ***on the totality of the record***." *Ex parte Wada and Murphy*, BPAI Appeal No. 2007-3733 (January 14, 2008), and "***Office personnel must articulate***", among other things, "***a finding that the prior art included each element claimed*** …", MPEP 2143 (A)(1). The "***unwitting application of hindsight" is inappropriate***. *Ex parte So and Thomas*, BPAI Appeal No. 2007-3967 (January 4, 2008). In other words, the Examiner's "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). (MPEP § 2142). (Emphasis added.)

For at least the foregoing reasons, Applicant respectfully submits that claim 1, as amended, is patentable under 35 U.S.C. §103(a) over any combination of Kanegasaki, Hanagan,

and/or Breznak.

Accordingly, claims 2, 3, 5-7, 9-25, 27-39, and 42-48, which depend from now allowable amended claim 1, are also patentable under 35 U.S.C. § 103(a) over any combination of Kanegasaki, Hanagan, and/or Breznak for at least this reason. Moreover, even assuming that these claims were not patentable by virtue of dependence from allowable claim 1, Applicant submits that claims 2, 3, 5-7, 9-25, 27-39, and 42-48 are patentable for at least the additional reason that none of the cited references to Griffith, Thomas, Sparks, Henkens, Quake, Rao, Allen, Anderson, Herman, and/or Turner, taken alone or in combination, cure the deficiencies of Kanegasaki, Hanagan, and/or Breznak.

Griffith, as understood by Applicant, discloses systems having "(1) a micromatrix and perfusion assembly suitable for seeding and attachment of cells within the matrix and for morphogenesis of seeded cells into complex, hierarchical tissue or organ structures, wherein the matrix includes channels or vessels through which culture medium, oxygen, or other nutrient or body fluids can be perfused while controlling gradients of nutrients and exogenous metabolites throughout the perfusion path independently of perfusion rate, and (2) sensor means for detecting changes in either cells within the matrix or in materials exposed to the cells, have been developed." (Griffith, Abstract.)

Thomas, as understood by Applicant, discloses an "apparatus for performing cell growth and cell based assays and methods for performing such assays." (Thomas, [0002].)

Sparks, as understood by Applicant, discloses "devices for determining the number of-bacteria present in liquid bacterial culture at varying intervals during the process of incubation and multiplication, and particularly to that type of device for counting the number of organisms present, based on the turbidity of the liquid media and culture." (Sparks, Abstract.)

Henkens, as understood by Applicant, discloses an "electrochemical detection system which specifically detects selected nucleic acid segments," where the system utilizes biological probes such as nucleic acid or peptide nucleic acid probes which are complementary to and specifically hybridize with selected nucleic acid segments in order to generate a measurable current when an amperometric potential is applied." (Henkens, Abstract.)

Quake, as understood by Applicant, discloses "microfluidic chromatography devices for separating an analyte from a sample solution, and methods for producing and using the same." (Quake, Abstract.)

Rao, as understood by Applicant, discloses a bioprocessing system that "relies on non-invasive optical chemical sensing technology wherein an optical excitation source excites an optical chemical sensor." (Rao, Abstract.)

Allen, as understood by Applicant, discloses a nanomotion sensor having a "micromechanical device for the detection and characterization of specimen motions when they interact with one or an array of cantilevered sensors set in the path of the moving specimen" and "a method for direct sensing and characterization of motion, including position, torsion, magnitude and direction of velocity, acceleration, force, torque, as well as binding." (Allen, Abstract.)

Anderson, as understood by Applicant, discloses a "miniaturized integrated nucleic acid diagnostic device and system which includes a nucleic acid extraction zone including nucleic acid binding sites." (Anderson, Abstract.)

Herman, as understood by Applicant, discloses "methods and devices in which living cells or subcellular biocatalysts are immobilized in an open chamber defined by two rotating disks." (Herman, Abstract.)

Turner, as understood by Applicant, discloses "a regenerable biosensor probe adapted for positioning in a bioreactor." (Turner, Abstract.)

None of the cited references to Griffith, Thomas, Sparks, Henkens, Quake, Rao, Allen, Anderson, Herman, and/or Turner, taken alone or in combination with Kanegasaki, Hanagan, and/or Breznak disclose all of the features recited in amended claim 1 of the present invention, and therefore amended claim 1 is also under 35 U.S.C. § 103(a) over any combination of these cited references for at least this additional reason.

Claims 49-63 and 65-75:

As set forth above, amended claim 49 recites "[a] bioreactor comprising:

(a) a substrate having a first surface and an opposite second surface; and

(b) a plurality of arrays of chambers formed on the substrate, each array being adapted for receiving cells in a liquid medium and comprising a channel and a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end, wherein at least two of the plurality of chambers have depths same or different from each other, ***and wherein for at least one array, each of the chambers is adapted to receive and culture at least one predetermined type of cells***;

(c) means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers of at least one array; and

(d) ***a barrier for at least one of the chambers of at least one array, wherein the barrier:***

(i) is positioned at the open end of the corresponding chamber proximate to the intersection of the channel and the corresponding chamber; and

(ii) has a porosity to allow the corresponding chamber and the channel to be in fluid communication, and to allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined type of cells not to permeate between the corresponding chamber and the channel." (Emphasis added.)

Incorporating herewith the reasons set forth above why amended claim 1 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak, Applicant submits that amended claim 49 is patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak for at least these reasons.

Accordingly, claims 50, 51, 53-55, 57-63, 65-75, which depend from now allowable amended claim 49, are also patentable under 35 U.S.C. § 103(a) over Kanegasaki, Hanagan, and/or Breznak for at least this reason. Moreover, even assuming that these claims were not patentable by virtue of dependence from now allowable amended claim 49, Applicant submits that claims 50, 51, 53-55, 57-63, 65-75 are patentable for at least the additional reason that none of the cited references to Griffith, Thomas, Henkens, Quake, Rao, Allen, Anderson, Herman and/or Turner, taken alone or in combination with Kanegasaki, Hanagan, and/or Breznak disclose, teach, or suggest all of the features recited in now allowable claim 49, as amended.

Claims 76 and 77:

As set forth above, amended claim 76 recites "[a] method for ***culturing a plurality of biofilms***, each containing a predetermined type of cells or cell growth conditions, comprising the steps of:

(i) providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality of arrays of chambers formed on the substrate, each array being adapted for receiving cells in a liquid medium and comprising a channel and a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end, and wherein at least two of the plurality of chambers have depths different from each other; and

(ii) ***culturing at least two biofilms in at least two arrays of chambers of the bioreactor***." (Emphasis added.)

In contrast, as set forth above and as understood by Applicant, Kanegasaki discloses "a

well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor." (Kanegasaki, [0009].) On page 12 of the Office Action, the Examiner concedes that "Kanegasaki does not disclose the use of biofilms." In other words, Kanegasaki does not disclose, teach, or suggest a method for ***culturing a plurality of biofilms***, each containing a predetermined type of cells or cell growth conditions, comprising the steps of "providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality or array of chambers formed on the substrate…and ***culturing at least two biofilms in at least two arrays of chambers of the bioreactor***" as recited in amended claim 76. (Emphasis added.)

Herman, as understood by Applicant, discloses "methods and devices in which living cells or subcellular biocatalysts are immobilized in an open chamber defined by two rotating disks." (Herman, Abstract.) Turner, as understood by Applicant, discloses "a regenerable biosensor probe adapted for positioning in a bioreactor." (Turner, Abstract.) Neither Herman not Turner, taken alone or in combination with Kanegasaki, disclose, teach, or suggest a method for ***culturing a plurality of biofilms***, each containing a predetermined type of cells or cell growth conditions, comprising the steps of "providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality or array of chambers formed on the substrate…and ***culturing at least two biofilms in at least two arrays of chambers of the bioreactor***" as recited in amended claim 76. (Emphasis added.)

Turner, as understood by Applicant, discloses "a regenerable biosensor probe adapted for positioning in a bioreactor." (Turner, Abstract.)

For at least the reasons set forth above, Applicant respectfully submits that the Examiner has failed to make a *prima facie* case to support the rejection of claim 76 under 35 U.S.C. §103(a) over Kanegasaki and/or Herman. First, there is no suggestion or motivation to modify the references or combine the reference teachings. Second, there is no reasonable expectation of success of combining the reference teachings. Finally, the combination of references does not teach or suggest all elements of Applicant's claims.

For at least the foregoing reasons, Applicant respectfully submits that claim 76, as amended, is patentable under 35 U.S.C. §103(a) over any combination of Kanegasaki and/or Herman.

Accordingly, claim 77, which depends from now allowable amended claim 76, is also patentable under 35 U.S.C. § 103(a) over any combination of Kanegasaki, Herman, and/or Turner for at least this reason.

CONCLUSION

Applicant respectfully submits that the foregoing Amendment places this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner's amendment, to facilitate the prosecution, please call the undersigned at 404.495.3678. No fee is due, but the Commissioner is hereby authorized to charge any petition fee under 37 CFR 1.17(f),(g) or (h) or any deficiency of fees and credit of any overpayments to Deposit Account No. 50-3537.

Respectfully submitted,

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September 17, 2010

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